

Anton Skrabal<sup>1</sup>, Otto Ringer<sup>1</sup>: The hydrolysis rate of orthoformic acid ethyl ether



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## THE HYDROLYSIS OF ORTHOFORMIC ACID ETHYL ETHER

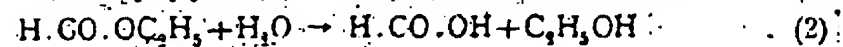
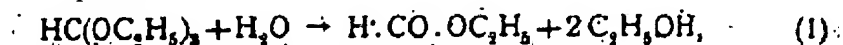
## Introduction

Chemical kinetics research is still far removed from knowing the time course of simple hydrolytic reactions of the various substance classes with an ethereal bonded oxygen atom. Up to now, orthocarboxylic acid esters, which are connected with important constitution problems and synthetic methods, have in no way been worked up with regard to the kinetics of their hydrolysis.

A beginning will be made here with esters of the simplest orthocarboxylic acid, the hypothetical orthoformic acid, and the hydrolysis of its ester that is most easily accessible, orthoformic acid ethyl ester  $\text{HC}(\text{OC}_2\text{H}_5)_3$ , will be investigated. According to its behavior during hydrolysis, which is the result of the investigation under consideration, this substance and presumably also the analog compounds with the chemical group  $-\text{C}(\text{OR})_3$ , where R signifies an alkyl, would be designated properly as ethers and not as esters, with this more proper designation already being selected in the title.

From the rather comprehensive preparative literature available regarding this compound and the closest homolog, orthoacetic acid ether, it was then possible to find a criterion satisfactory enough to guide our work: during the hydrolysis--and we are still talking only about a hydrolysis brought about by acids--it was always possible to find, as degradation products, only bodies with an alkoxy group--namely, esters of the usual concerned acids--that is, formic acid, or acetic acid esters, or their decomposition products, acid and alcohol.

It should therefore be assumed that the hydrolysis of orthoformic acid ether would be calculated as a consecutive reaction with only one intermediate stage, in accordance with the following reaction equations:



--an assumption also confirmed by the experiment.

The rate of the second reaction, the saponification of the formic acid ester, in its dependence on the concentration of the ester and the ions  $\text{H}^+$  and  $\text{OH}^-$  of the water, is already known [1]. Therefore, one had to determine the rate of the first reaction. According to explanations made by R. Wegscheider [2], it was basically the determination of the constants of three secondary reactions, the aqueous saponification, the alkaline saponification, and the acidic saponification, in which constants--since the work was carried out in aqueous solution--it is possible to include the constant water concentration.

As regards the analysis feasibility of the reaction mixture as a prerequisite for the feasibility measuring of the reaction and the change in acidity, which occurs as a result of the reaction course and which influences the saponification rate, one can say the following. The first of the two secondary effects takes place without an "acid toning"; its course therefore changes nothing in the rate of the acidic and alkaline saponification. The second reaction releases an acid; its course therefore delays the alkaline saponification and favors the acidic saponification. The conversion after the second reaction results from the titration of the produced formic acid; the conversion after the first reaction, from the produced formic acid and the produced formic acid ester. The latter can be calculated accurately and quickly thanks to its very rapid alkaline saponification, by excess alkali, which saponifies it, and back-titration with acid. The prerequisite for the application feasibility of this analysis method is a corresponding resistance of ortho ethers with respect to alkali.

In order to test this assumption, we had to therefore first investigate the behavior of the ortho ether in a correspondingly alkaline medium.

The used orthoformic acid ethyl ether was a Kahlbaum preparation, always purified shortly before its use by fractional distillation. The measurements were carried out in a thermostat at 25°.

Therefore, the ortho ether was first introduced into a sodium carbonate solution and by titration of the soda with 0.1N HCL, relative to bicarbonate, the change in titer was determined [3]. The experiment, which extended over a week, produced only slight decreases in titer. With regard to the very rapid alkaline saponification of the formic acid ester, only traces of the latter can be present in the reaction mixture. After its formation after the first reaction, it must be further saponified at a superior rate under the conditions of our experiment. The rate of the titer decrease is, therefore, essentially indicated by the rate of the saponification of the ortho ether.

In order to test whether the slow saponification of orthoformic acidic ethyl in the soda solution is an aqueous saponification, an acidic saponification, or an alkaline saponification, the ortho ether was introduced into a 0.1N sodium hydroxide solution and its titer decrease was determined with acid and phenolphthalein as the indicator. In this medium, the formic acid ester, which forms slowly according to equation (1), leaves even more rapidly than in the soda solution, and the titer change of the sodium hydroxide indicates the direct conversion of the ortho ether. In the case of the aqueous saponification, the same rate was then to be predicted as in the soda solution--in the case of the acidic saponification, a delayed rate, and in the case of the alkaline saponification, an accelerated rate. The experiment produced constancy of the hydroxide titer for one week. A very slight titer decrease, which could just be observed, is sufficiently explained by the unavoidable absorption of atmospheric carbonic acid by the sodium hydroxide.

Thus, on the one hand, it was made probable that the ortho ether in the soda solution was acidically saponified; on the other hand, it was determined that the orthoformic acidic ethyl is not subject to an alkaline saponification or an aqueous saponification either--in any case, not in the amount of the otherwise previously found orders of magnitude, an [illegible], which is to be understood in principle and is presupposed by the degree of accuracy of the analysis methods and the duration of the measurements.

If the reaction in the soda solution really is an acidic saponification, a tremendously rapid reaction of the ortho ether was to be expected for a mineral acid solution.

The saponification was therefore investigated in a 0.1-norm hydrochloric acid-acidified solution and the measurement method was set up so that the first stage of the secondary effects, the reaction of the ortho ether to formic acid ester, was revealed. A reaction mixture was prepared that contained 0.1 mol ether and 0.1 mol HCl; samples of this were taken from time to time, and allowed to flow into small flasks, in which there was an excess quantity of 0.1-norm barite, and they were closed with cork plugs with soda lime tubes.

The saponification of the ortho ether had to be at a standstill at the time it was made alkaline; on the other hand, the formic acid formed from it--to the extent that it, in turn, had not been subjected to acidic saponification--had to be subjected to alkaline saponification very rapidly. The titer decrease of the hydroxide present therefore had to correspond to the sum from the formic ester and the formic acid and thus to the quantity of ortho ether consumed in the reaction, after the deduction of the amount for the catalyst acid.

The titer decrease of barite hydroxide always exhibited, both with the sample immediately taken after the preparation of the reaction mixture and also with all later samples, a quantity of consumed ortho ether which was equal to its initial concentration. The experiment was repeated--in order to be very certain--but the first sample taken immediately at the beginning of the reaction always indicated complete conversion of the ortho ether.

The hydrolysis of ortho ether to formic acid ester in mineral acid solution therefore takes place very rapidly. This also had to be demonstrable in a completely different way.

The hydrolysis of the formic acid ester takes place at a moderate, exactly known rate, in mineral acid solution. If ortho ether is reacted in the acidic medium, the case of a two-stage reaction was therefore present, in which the first stage takes place at an outstanding rate, in comparison to the second one; the experiment can be shown by the one-stage rate equation of the slower partial reaction. Therefore, if a measurement method was applied toward the same reaction mixture, which was based on the following of the conversion according to the second stage, the measurement of the produced formic acid, then the result would have to be the already known rate constant of the formic acid ester according to the one-stage monomolecular calculation.

The reaction of the formic acid ester and the orthoformic acid ether in hydrochloric acid solution

The exact measurement of the constants of the acidic saponification of the formic acid ester was done by Palomaa (l. c.) and involved a difficulty which, as in many similar cases, is found in the rapid alkaline saponification of the ester. If one turns namely to the acid titer soda and phenolphthalein determinations, then an increased consumption occurs due to the alkaline saponification of ester still present at the titration endpoint and with the local excess of titer solution at the site of influence.

In such cases, ammonia [4] was frequently selected, which, as a weak base, does not exhibit this disadvantage, but instead makes the titration less exact. Palomaa sought a way out in the middle in that he used the stronger ethylamine.

According to the design of the titration experiment by N. Bjerrum [5], however, the use of weak bases and acids as measurement solutions does not cause any difficulties, and the work is carried out with the best--that is, determined--titration exponents. We therefore used ammonia and 6.35 as the best titration exponents, for which p-nitrophenol is a suitable indicator. The titration error is then  $0.03 \text{ cm}^3$  at the beginning and  $0.1 \text{ cm}^3$  at the end of the measurement, or 1%, or 2% of the current ester concentration--this is, it corresponds to the desired accuracy.

The titration of Experiment 1 was carried out in this way. In Experiments 2 to 5, the work was more rapid and simple, in that alizarine was used as an indicator and the titration was pale yellow to purple [6]. The accuracy of this simplified experiment is, as the experiment teaches, also sufficient.

For the rest, the procedure was very similar to that used by Palomaa, only the reaction was undertaken in larger quantities, in that  $500 \text{ cm}^3$  reaction mixture were prepared and samples of  $50 \text{ cm}^3$  were titrated.

## Experimental series 1

### Formic acid ethyl ester in hydrochloric acid solution

#### Experiment 1

$$\xi = 0.09948, S = 0.09934$$

$t$	$\xi - x$	$k$	$k$
0	0.07070	—	—
15	0.05982	0.0193	0.0193
25	0.04918	0.0192	0.0193
42	0.03518	0.0197	0.0195
60	0.02520	0.0185	0.0192
78	0.01778	0.0193	0.0192
105	0.01072	0.0187	0.0192

① Mittel... 0.0191

$k$  für  $S = 1 \dots 0.192$

②

Key: 1 Average  
2 For

### Experiment 2

$$\xi = 0.11255, S = 0.00917$$

$t$	$\xi - x$	$k$	$k$
0	0.10230	—	—
5	0.08844	0.0189	0.0182
16	0.07658	0.0180	0.0181
26	0.06362	0.0186	0.0183
38	0.05102	0.0184	0.0183
54	0.03836	0.0178	0.0182
83	0.02304	0.0176	0.0180

① Mittel... 0.0181

$k$  für  $S = 1 \dots 0.183$

②

Key: 1 Average  
2 For

### Experiment 3

$$\xi = 0.10835, S = 0.09920$$

$t$	$\xi - x$	$k$	$k$
0	0.10042	—	—
7	0.08844	0.0181	0.0181
14	0.07768	0.0186	0.0183
22	0.06882	0.0188	0.0185
33	0.05474	0.0182	0.0184
50	0.03908	0.0185	0.0184
82	0.02242	0.0181	0.0183
134	0.00879	0.0180	0.0182

① Mittel... 0.0183

$k$  für  $S = 1 \dots 0.185$

②

Key: 1 Average  
2 For

## Experimental series II

Orthoformic acid ethyl ether in hydrochloric acidic solution

## Experiment 4

$\xi = 0.12935, S = 0.09788$

$t$	$\xi - x$	$k$	$k$
0	0.12014	—	—
8	0.10282	0.0195	0.0195
16 <sup>45/60</sup>	0.08660	0.0193	0.0194
27 <sup>50/60</sup>	0.07002	0.0194	0.0194
40	0.05548	0.0191	0.0193
55	0.04200	0.0188	0.0181
78	0.02740	0.0186	0.0189
118	0.01260	0.0194	0.0191
(1) Mittel...		0.0191	
(2) $k$ für $S = 1$ ...		0.195	

Key: 1 Average  
2 For

## Experiment 5

$\xi = 0.10455, S = 0.09831$

$t$	$\xi - x$	$k$	$k$
0	0.09652	—	—
7	0.08428	0.0194	0.0194
15	0.07248	0.0189	0.0191
26	0.05880	0.0190	0.0191
39	0.04630	0.0184	0.0183
56	0.03354	0.0190	0.0180
77	0.02258	0.0188	0.0189
(1) Mittel...		0.0189	
(2) $k$ für $S = 1$ ...		0.192	

Key: 1 Average  
2 For

In the tables,  $S$  signifies the concentration of the catalyst acid (hydrochloric acid), which, like all other concentrations, is indicated in moles per liter;  $\xi$ , the equilibrium concentration of the produced formic acid or the saponifiable fraction of the ester [7];  $\xi - x$  the current concentration of the saponifying ester, determined from the current acid titer and  $\chi$ ; and  $t$ , the time in minutes.

The rate constant was calculated according to the formula:

$$k = \frac{1}{t_2 - t_1} \ln \frac{\xi - x_1}{\xi - x_2}$$

--one time from two directly successive values of  $t$  and  $\epsilon$ , that is, according to the sequence formula [8], and the other time, in the most common manner, according to the step formula, which strips away the errors.

The average value of the constant, related to  $S = 1$ , of the acidic saponification of the formic acid ester from all three experiments is 0.187 and completely agrees with the one found by Palomaa. The best value, however, should be that of Experiment 1, since it is based on the most accurate titration method (titration with a determined titration exponent). We therefore want to hold on to the value:

$$k = 0.192 \text{ (25°).}$$

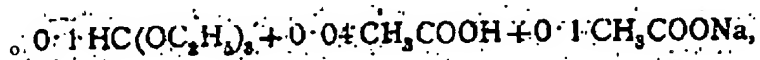
Experiments 4 and 5 with the orthoformic acid ethyl ether finally produced a good constancy of  $k$  and for the value, related to  $S = 1$ , of the constant on average  $k = 0.1983$ --that is, the same value as for the formic acid ethyl ester.

Thus, it appears to be proved that the orthoformic acid ethyl ether is converted into formic acid ester at an unmeasurably rapid rate in a strongly acidic solution.

#### Experiment plan for the measurement of the rapid reaction

Since reaction (1) takes place unmeasurably fast in  $[H^+] = 0.1$  solutions, but in  $[H^+] = 0.1$  or  $[H^+] = 10^{-13}$  solutions is practically stationary, it was predictable that it progresses, with an average acidity, at a rate that can be easily measured. It was also obvious that the most suitable acidity should be sought by using various hydrogen ion buffers.

In order to slow the acidic saponification of the ortho ether, it was first undertaken in the reaction mixture (gram formula weights per liter):



that is, with the acidity  $[H^+] = 7.2 \cdot 10^{-6}$ . The measurement method was the same as the one implemented at the beginning: taking of a sample in excess hydroxide and measurement of the formic ester produced from the ortho ether. The first measurement, undertaken immediately after the start of the reaction, produced a result of 50%. The hydrolysis is therefore also too fast at this acidity for measurement.

Thus, there was a case of hydrogen ion catalysis of a speed so unusual that up to now, it had not yet been observed in acidic saponifications.

The acidic saponification in the acetic acid-acetate solution again justifies the assumption stated in the beginning, wherein the slow reaction observed in the soda solution is an acidic saponification.



The attempt was recently made to measure the reaction in a carbonate solution, wherein to increase the rate, a copious bicarbonate additive was used. In fact, the decrease in soda titer was then a noticeably more rapid decrease but a sign that the ortho ether was actually acidically saponified in the soda solution; however, we soon abandoned those experiments: the reaction was still too slow to give useful results and moreover, the carbonate-bicarbonate buffer with a high bicarbonate concentration cannot withstand an experimental time of many days [9].

Something similar is true for an ammonia-ammonium salt buffer, which permits the reduction of the acidity to  $[H\bullet] = 10^{-[illegible]}$ .

Thus, two paths appeared to be still open, wherein by following these paths, a suitable reaction rate was promised: the selection of a buffer with the range around  $[H\bullet] = 10^{-6}$  or one around  $[H\bullet] = 10^{-7}$ .

The former path proved less feasible. To be sure, with  $[H\bullet] = 10^{-8}$ , abandoning the formal standpoint would have been particularly attractive. As can be seen from the finally determined numerical value of the constant of the ortho ether and the already known one of the acidic and alkaline saponifications of the formic acid ester, the two-stage reaction would really appear here as such. Both partial reactions would have had rates of the same order of magnitude; the first would be the acidic saponification of the ortho ether without acid toning and would have been accelerated by hydrogen ions; the second, the alkaline saponification--the acidic saponification would have been neglected--of the formic acid ester with acid toning and would have been delayed by hydrogen ions. The mathematical expression of the entire process would be a system of simultaneous differential equations of the following form:

$$\left. \begin{aligned} \frac{dx}{dt} &= k_1(a-x) \frac{c+y}{b-y} \\ \frac{dy}{dt} &= k_2(x-y) \frac{b-y}{c+y} \end{aligned} \right\}$$

Without going into the question of the integration of the system or the further possibilities of operating with these equations, one can say that all methods would have made available mathematical expressions of such complexity that their use with regard to the expected accuracy of the analysis results appeared to be of very questionable value. As a result of the simultaneously present buffer salts, a large alkali excess had to be taken, namely, for the determination of the formic acid ester, so that  $x - y$  is determined as a small difference, that is, not very accurate. Moreover, especially in the area  $[H\bullet] = 10^{-8}$ , there is a lack of a buffer of normal useability.

In this case, like in many similar cases, working toward the simplest and most transparent conditions possible is urgently recommended. Such conditions are given by the acidity  $[H\bullet] = 10^{-7}$ --that is, the measurement of the reaction in the neutrality areas.

Here, a phosphate buffer from primary and secondary phosphate is available. The dissociation constant of the phosphoric acid after the second stage is  $1.95 \times 10^{-7}$ , or with sufficient accuracy,  $2 \times 10^{-7}$ ; the surroundings of a hydrogen ion concentration of numerical value therefore had to be taken into consideration. As a rough calculation showed, the alkaline saponification of the formic acid ester had to take place here very slowly already. Thus it was possible to strive for a very substantial simplification of the conditions. If the reaction of the ortho ether took place so rapidly that the saponification of the formic ester, which influences the acidity, could probably be neglected for the duration of the reaction course which was followed, then an isolation of the reaction of the first step, which is what we are dealing with, and which takes place without acid toning, was attained in a medium of constant acidity--therefore, the simplest time law, the one-stage equation of first order, is applicable to the time process to be measured.

Of the reaction partners, only one was to be analyzed here, the produced formic acid ester, and this could occur only by the alkaline saponification of the latter by an added corresponding excess of hydroxide, wherein the reaction to be measured was appropriately slowed down with an excess, and a subsequent back-titration to secondary phosphate.

In order to find out now whether these desirable experimental conditions could really be implemented, one had to find a clue for the rate at which the ortho ether reacts here, and thus, on the basis of these assumptions and without consideration as to whether they are exactly fulfilled, some orienting preliminary experiments were first carried out with a ratio of the buffer 1:1--that is, with an acidity  $[H\bullet] = 2 \times 10^{-7}$ ; the possible errors could, in no way, be so large as to be able to at least determine the order of magnitude of the rate of the reaction.

These preliminary experiments showed that the reaction course, in fact, took place in a few hours and produced, as a rounded-off, approximate numerical value, the constant 50,000, relative to  $[H\bullet] = 1$ .

The meanings are as follows:

k	constant of the acidic saponification of the ortho ether for $[H\bullet] = 1$ .
$k_a$	constant of the alkaline saponification of the formic ester for $[H\bullet] = 1$ .
$k_2$	dissociation constant of the phosphoric acid according to the second stage.
$k_3$	dissociation constant of the phosphoric acid according to the third stage.
a	starting concentration of the ortho ether.
$\pi$	starting concentration of the primary phosphate.
$\sigma$	starting concentration of the secondary phosphate.

$h$	hydrogen ion concentration.
$w = 10^{-14}$	water constant for 25°.
$x$	conversion variable of the first reaction.
$y$	conversion variable of the second reaction.

For  $k$ , the orientation value  $k = 5 \times 10^4$ , for  $k_a$ , the value [10]  $k_a = 1400$  was used.

Because it is simply a matter of the determination of the best experimental conditions, one can be satisfied with approximate numerical values.

For the beginning of the reaction, the following is valid:

$$h = k_2 \frac{\pi}{\sigma} \quad (3)$$

In the course of the reaction, a quantity  $y$  of formic acid is formed; it is stronger than the phosphoric acid after the second stage and converts  $y$  moles of the secondary phosphate into primary phosphate. Therefore, the following is valid for the current acidity:

$$h = k_2 \frac{\pi + y}{\sigma - y} \quad (4)$$

By setting  $k$  as a constant according to (3), we produce an error  $F$ . It amounts to the following in percentage:

$$F = \frac{k_2 \frac{\pi + y}{\sigma - y} - k_2 \frac{\pi}{\sigma}}{k_2 \frac{\pi}{\sigma}} \cdot 100 = \frac{y(\pi + y)}{\pi(\sigma - y)} \cdot 100 \quad (5)$$

In order to determine this error in an arbitrary stage of the reaction--that is, for an arbitrary value of  $z$ , we need to know the relation between  $y$  and  $x$ , and because  $F$  should be small, then one can be satisfied with an approximate relation. The approximation that we make and that is fulfilled all the better, the smaller  $F$  or the more changeable  $h$  is, is that we neglect  $y$  as small, in comparison to  $x$ ,  $\pi$  and  $\sigma$ . Then, our simultaneous differential equations are simplified and become:

$$\left. \begin{aligned} \frac{dx}{dt} &= k h (a - x), \\ \frac{dy}{dt} &= k_a \frac{w}{h} x, \end{aligned} \right\} \quad (6)$$

where  $h$  has the value according to (3).

Then, by division, it follows that:

$$\frac{dy}{dx} = \frac{k_o n}{k h^2} \cdot \frac{x}{a-x}$$

and integrated:

$$y = \frac{k_o n}{k h^2} \{ a-x-a \ln (a-x) \} + J.$$

The integration constant J follows from  $y = 0$  for  $x = 0$ . Their use finally produces the following as the sought relation:

$$y = \frac{k_o n}{k h^2} \left\{ a \ln \frac{a}{a-x} - x \right\}. \quad (7)$$

According to this expression, the  $y$  for arbitrary  $a$ ,  $x$  and  $h$  can be calculated and by the use of  $y$  in (5), the error  $F$ , in its dependence on  $y$  and the buffer salt quantities  $\pi$  and  $\sigma$ , can be determined.

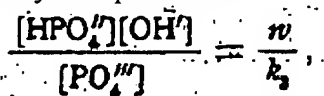
This was carried out for a number of cases, and sufficiently small values of  $F$  resulted for a number of them.

The results obtained were evaluated for the experimental conditions to be established, taking into consideration the viewpoints which are to follow.

The only possible type of analysis was already characterized. The main thing was to manage with the lowest possible hydroxide excesses, if the analysis result, as a small difference, was not to be very inaccurate.

Standing in the way of this was the presence of the buffer salt. The lower the quantities of buffer salts to be used, the lower would be the hydroxide quantity. They should not be selected too small, however, since from (5), it is clear that  $F$  is all the smaller, the larger the  $z$  and  $\pi$  and  $\sigma$ . Between these contrary considerations, therefore, a middle course would have to be sought and found.

The hydroxide excess was to be dimensioned in such a way that the formic ester to be analyzed saponifies quantitatively in a short time. With a small hydroxide excess, it first saponifies in the excess hydroxide and then, when this is consumed, in a mixture of secondary and tertiary phosphate. The reaction time for the ester saponification is sufficiently dimensioned if we calculate it for the alkalinity which prevails at the end of the reaction. This alkalinity follows, in accordance with the hydrolysis equilibrium:



from the following quadratic equation:

$$[\text{OH}'] = \frac{n}{k_s} \cdot \frac{T - [\text{OH}']}{S + [\text{OH}']}$$

or:

$$[\text{OH}]^2 + \left(S + \frac{n}{k_s}\right)[\text{OH}] - \frac{n}{k_s}T = 0, \quad (8)$$

where S and T signify the "analytical concentrations" of the secondary or tertiary phosphate.

If we assume the formic ester to be saponified if it has been reacted to 99%, then the reaction time R is calculated in minutes for the alkalinity  $[\text{OH}']$ , in accordance with the following equation:

$$k_a[\text{OH}]R = \ln 100. \quad (9)$$

The hydroxide excess was so dimensioned that R is only fractions of a minute. Since the formic ester first saponifies in an essentially alkaline medium, this statement is surely much too generous; however, one is soon convinced that there is not much to spare here.

From these explained viewpoints, a series of experimental conditions were weighed, and the following were selected as the most suitable:

	① Versuchsreihe A	② Versuchsreihe B
a.....	0.1	0.1
x.....	0.03	0.06
α.....	0.08	0.08
h (3).....	$1 \times 10^{-1}$	$2 \times 10^{-1}$
r.....	0.07	0.09
y (7).....	0.0014	0.00098
F (5).....	7.2	3.3
L.....	0.14	0.20
S.....	0.05	0.07
T.....	0.04	0.05
$[\text{OH}]$ (8).....	0.013	0.013
R (9).....	0.25	0.25

Key: 1      Experimental series A  
 2      Experimental series B

The error which was calculated from (5) and which flows from the inconstancy of the acidity appears indicated here for that x up to which the reaction was followed by measuring--that is, for the end of the measuring. For the middle and beginning of the

measurement, it is, of course, substantially less, so that the acidity, with sufficient accuracy, should be assumed as constant.

L is the hydroxide quantity used for fixing the reacting system and for saponification of the produced formic ester. It is, like the other concentrations, indicated in moles per liter in the table.

The measurement of the acidic saponification of the ortho ether

The titration was done according to the data from Bjerrum for secondary phosphate--for a titration exponent 9.57, and using a Soerensen standard solution, dyed with the indicator. 13 drops of a 1% alcoholic phenolphthalein solution was used on 100 cm<sup>3</sup> of the latter and the titrated-out solution.

With this titration exponent, an acidic saponification of the ortho ether was not to be feared; on the other hand, the use of a strong acid as the standard solution had to be avoided, considering the local acid excess on the influence site, which could lead to an acidic saponification of the ortho ether. The latter takes place without acid toning, that is, would be, in fact, without disadvantageous effect, but leads to the formic ester, the latter of which is subjected to an alkaline saponification in the solution to be titrated and would bring about an erroneous reduced consumption of titration acid. For this reason, 0.1-norm acetic acid was used as the standard solution, which was without importance for the accuracy of the titration, since the dissociation constant of the acetic acid is substantially greater than  $k_2$  of the phosphoric acid.

The execution of the experiments took place in the following manner:

As buffer salts, the Kahlbaum preparations  $\text{KH}_2\text{PO}_4$  and  $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$  "according to Soerensen" were used. The weighed quantities were dissolved in a volumetric flask to 500 cm<sup>3</sup> in boiled water and the ortho ether, weighed in by means of a Rey pipette, was added to the reaction flask, filled to the mark; it was quickly brought to 25° and the reaction flask was suspended in the thermostat.

The reaction flask was provided with a lifting apparatus which could be closed, which permitted taking samples with the smallest possible evaporation losses. They were captured in a volumetric flask to 50 cm<sup>3</sup> and from this, brought to a beaker (time reading), in which the required quantity of hydroxide had already been added from an automatic pipette. After waiting for some time (1/4 minute, see above), the back-titration with acetic acid took place.

The calculation was carried out according to the following formula:

$$k h = \frac{1}{t_2 - t_1} \ln \frac{a - x_1}{a - x_2} \quad (10)$$

The method, as it was described, did not allow us to expect any special accuracy, since despite all limitation, one had to work with sizeable hydroxide excesses; the current

concentration  $a - x$ , therefore, came out as a small difference. In addition, there are the unavoidable mistakes, as a result of the effect of atmospheric carbonic acid, which is always connected with investigations in which one must deal with strongly alkaline solutions for some time.

Finally, another error source was taken into consideration, whose influence could not yet be extensively eliminated, and which suppressed the degree of accuracy by another stage. This was the evaporation of the formic acid ester, which, by itself, boils at  $54^\circ$  and has a high partial vapor pressure in the  $25^\circ$  reacting mixture.

This fact of the accurate measurement of the acidic and alkaline saponification of that ester is not very restricting. With these rapid reactions, the concentration of the volatile reaction partner decreases rapidly with time, with the formation of nonvolatile reaction products, which are measured. Here, however, the concentration of the volatile substance increases with time and has the greatest values toward the end, that is, in the second unequally longer parts of the reaction, and the volatile substance being formed is used for the measurement of the reaction progress.

The mode of sampling mentioned above could also only reduce but not eliminate this evil, since with the length of the reaction and the gradual emptying of the reaction flask, the air space in the latter and thus the evaporation are greater and greater.

The loss as a result of the evaporation can also be seen from the experimental tables for the values indicated there for the time infinity. The way out, which is often selected in such cases, namely, to determine the current concentrations not from the starting values, but rather from the end value, was not feasible here, because, in fact, the concentration of the reacting substance was not reduced by the evaporation, but rather the concentration of the volatile reaction product to be measured.

In the following tables,  $a$  signifies the weighed quantity of ortho ether, which was the basis of the calculation;  $X_{\infty}$  the quantity of formic ester found by analysis at the end of the reaction. Because a reverse reaction is certainly not present,  $X_{\infty} = a$  should have been expected. As a result of the evaporation,  $X_{\infty} < a$  was found. The described phenomenon is manifested, above all, in a strong decrease of the constant in the last fourth of the reaction. In Experimental Series B, whose reactions were followed longer, the gradient is shown more clearly than in Experimental Series A. The constant values found too small as a result of the evaporation were placed in parentheses in the tables and were omitted in the calculation of the average. In the following, we have the measurements.

Experimental Series A

$$k = 1 \times 10^{-1}$$

## Experiment 6

$$a = 0.10949, \quad x_{\infty} = 0.10288$$

$t$	$a-x$	$kh$	$kh$
0	0.08859	—	—
23	0.08254	0.0071	0.0071
57	0.06631	0.0069	0.0069
94	0.05195	0.0068	0.0069
153	0.03497	0.0067	0.0068

$$kh = 0.00670$$

## Experiment 7

$$a = 0.11700, \quad x_{\infty} = 0.10576$$

$t$	$a-x$	$kh$	$kh$
0	0.10550	—	—
23	0.08958	0.0071	0.0071
47	0.07684	0.0068	0.0067
82	0.06084	0.0065	0.0067
125	0.04580	0.0066	0.0066
155	(0.03210)	(0.0059)	(0.0064)

$$kh = 0.00661$$

## Experiment 8

$$a = 0.11340, \quad x_{\infty} = 0.10590$$

$t$	$a-x$	$kh$	$kh$
0	0.0952	—	—
21	0.0835	0.0062	0.0062
46	0.0703	0.0069	0.0069
77	0.0564	0.0071	0.0068
118	0.0423	0.0070	0.0069

$$kh = 0.00685$$

## Experiment 9

$$a = 0.11203, \quad x_{\infty} = 0.10448$$

$t$	$a-x$	$kh$	$kh$
0	0.10643	—	—
19	0.09369	0.0062	0.0062
46	0.07637	0.0075	0.0070
77	0.06255	0.0084	0.0068
115	0.04883	0.0066	0.0067
160	0.03433	0.0064	0.0066

$$kh = 0.00669$$

## Experimental Series B

$$h = 2 \times 10^{-1}$$



## Experiment 10

$$a = 0.00733, \quad x_{\infty} = 0.08986$$

$t$	$a-x$	$kh$	$kh$
0	0.08405	—	—
15	0.08807	0.0141	0.0141
53	0.03987	0.0141	0.0141
81	0.02685	0.0144	0.0142
117	(0.01847)	(0.0102)	(0.0129)
168	(0.01259)	(0.0078)	(0.0114)

$$kh = 0.01415$$

## Experiment 11

$$a = 0.10527, \quad x_{\infty} = 0.09821$$

$t$	$a-x$	$kh$	$kh$
0	0.08927	—	—
9	0.07903	0.0135	0.0135
20	0.06705	0.0149	0.0143
34	0.05535	0.0137	0.0141
89	0.03541	0.0127	0.0134
100	0.02451	(0.0119)	(0.0120)
136	0.01709	(0.0120)	(0.0120)

$$kh = 0.01373$$

The first series  $kh$  was always calculated by interval integration; the second, by integration from the very beginning. The average values of  $kh$  were calculated from all combinations of all measurement results not placed in parentheses.

Better constancy of  $kh$  within the individual experiments could not be expected according to the cited error sources.

The values of the experimental series A give, in turn, the following as the average:

$$kh = 0.00674 \quad (h = 1 \times 10^{-7})$$

and the two of the experimental series B:

$$kh = 0.01394 \quad (h = 2 \times 10^{-7})$$

Therefore, they are also like the acidity in the ratio 1:2, with a deviation of only approximately 3%.

Thus, it appears to be proved that the hydrolysis of the orthoformic acid ethyl ether to formic acid ethyl ester can be calculated as a one-stage reaction, whose rate is proportional to the concentration of the ortho ether and hydrogen ion.

If one relates the rate to the concentration unit of the ortho ether and hydrogen ion, one obtains  $6.85 \times 10^4$ , or rounded off:

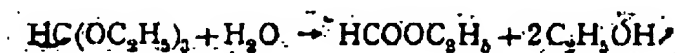
$$k = 70,000 (25^\circ)$$

From this, a midpoint of  $[H^+ = 0.1]$  minutes follows for  $1 \times 10^{-4}$  or--for the result as 99%--a reaction time of  $6 \times 10^{-[illegible]}$  minutes, in agreement with the results of the measurements in 0.1-norm HCl solution.

The results of the preliminary experiments also agree with the numerical value of the constant. On one hand, 1 minute is calculated from it, namely for the mid-point in the acetic acid experiment ( $h = 7 \times 10^{-6}$ ); on the other hand, for the result as only 10%, a reaction time of 20 days for the carbonate-bicarbonate experiment ( $h = 6 \times 10^{-11}$ ) and of 10,000 days for the hydrolysis by 0.1N NaOH ( $h = 10^{-13}$ ).

The chemical nature of the ethyl orthoformate

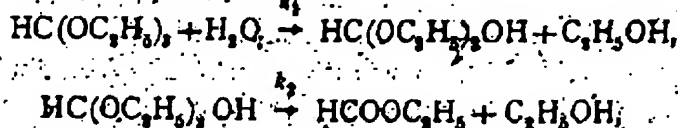
According to the result of our measurements, the orthoformic acid ether thus reacts in the sense of the following equation:



at a rate  $h$ , which is proportional to the hydrogen ion concentration. For  $[H^+] = 1$ ,  $k$  has the tremendous value of 70,000.

The question of whether this rapid acidic hydrolysis takes place directly, at one go, or via intermediate stages, remains unanswered. Both assumptions are compatible with the results of the measurements. The "chemical feeling" is an argument for the stagewise course. The tendency to assume stagewise reactions in the present case and in similar cases corresponds to our current molecular-kinetic views, based on probability-theoretical views and supported by general experience.

If we follow this tendency, we would have assumed at least two stagewise reactions:

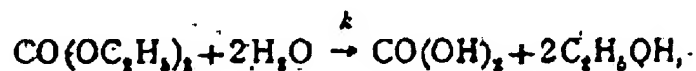


where between  $k_1$  and  $k_2$ , equations would have to be valid, which have such a nature that in measurements, the stagewise sequence with the constants  $k_1$  and  $k_2$  behaves exactly as the direct reaction with the constant  $k$ . There are two relations which satisfy this condition,

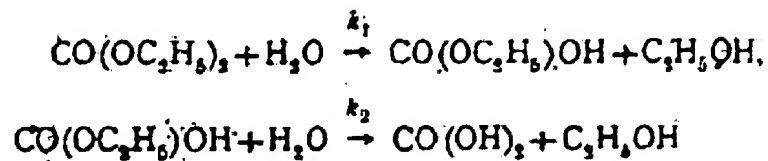
1st case. The constant  $k_1$  is very large in comparison to  $k_2$ . The orthoformic acid ester is converted into the intermediate substance  $\text{HC}(\text{OC}_2\text{H}_5)_2\text{OH}$  relatively rapidly and what is measured is the conversion of the latter into formic ester. The measured constant  $k$  is  $k = k_2$ . The circumstance that the intermediate substance could neither be isolated nor proved up to know speaks against this hypothesis. Since neither formic ester nor its saponification products are formed in the alkaline-rendered medium,  $k_2$  can be only very small in this medium. By dissolving the ortho ether in dilute acid and the immediate alkalinization of the solution, the ortho ether would have been converted almost completely into the intermediate product and it should have been possible to detect the latter then and, for example, to isolate it by vacuum distillation. That the preparative art has not yet succeeded in doing this speaks against the assumption  $k_1 \ll k_2$ .

2nd case. The constant  $k_1$  is very small in comparison to  $k_2$ . The ortho ether forms the intermediate product  $\text{HC}(\text{OC}_2\text{H}_5)_2\text{OH}$  relatively slowly; it is reacted to formic ester, in turn, relatively fast. The measured constant  $k$  is  $k = k_1$ . That the intermediate substance has not yet been detected, not to speak of being isolated, speaks in favor of the assumption  $k_1 \ll k_2$ ,

However, direct observations made with another substance which has hydroxyl and alkoxyl bonded to the same carbon speak for  $k_1 \ll k_2$ . We are referring to the saponification of the carbonic acid [11]. This reaction also takes place like a one-stage reaction, according to the measurements:



which, just like the hydrolysis of the formic acid ortho ether, can be thought as broken down into the stage sequence.

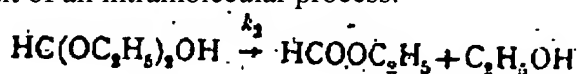


Here, however, we have the possibility of exposing the second of the two stagewise reactions in that it is possible to prepare the intermediate substance in the form of a sodium salt and to investigate it directly with regard to its reactivity. If one brings this sodium salt into aqueous solution, then the experiment teaches that it reacts with all ratios--that is, with any acidity taken into consideration--almost instantaneously to form carbonic acid and alcohol.

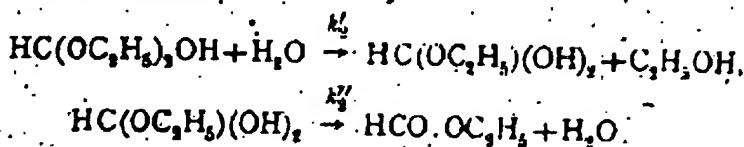
If we accordingly break down the measurable reaction of the saponification of the carbonic acid ester into a stagewise sequence, then as regards the constants of the stage sequence,  $k_1 \ll k_2$  and  $k = k_1$  are necessarily linked to this breakdown, as additional conditions.

The conditions with the carbonic acid ester and the additional circumstance that very generally, the monoalkyl and monoaryl derivatives of the geminal glycols "are mostly difficult to understand" [12] are an argument for the fact that we have also assumed that  $k_1 \ll k_3$  and  $k = k_1$  for the stage sequence of the ortho formic acid ether hydrolysis as probable.\*

Analogous with the carbonic acid ester, the rapid reaction, according to the second stage, can also be either the result of an intramolecular process:



or that of another stagewise sequence:



with our ortho ether also, wherein it was not possible to reach a decision.

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\*[Molecular-kinetically, one has thus said the following. It is the stagewise reaction of a substance with two identical and identically bonded reactive groups X. Such a substance has the structural formula XAAX, It reacts according to the following stagewise scheme:



If one designates with  $u$  the constant of the group rate of the substance XAAX--that is, the speed at which a certain group X of this substance reacts, then the rate  $k_1$  at which one or the other group reacts in XAAX is  $k_1 = 2u$ . With regard then to the rate  $k_2$  after the second stage, then one should distinguish here among three cases:

1. The reaction of the group X takes place independently--that is, (see R. Wegscheider Monatshefte für chemie, 9 (1908), 91 and 36 (1915), 471), uninfluenced whether the second group X is still present or is already replaced by X. Then,  $k_2 = u$ .

This case is, among other things, realized in the acidic saponification and esterification of the normal oxalic acid homologs and tartaric acid and in the acidic and alkaline saponification of the esters of ethylene glycols. In the electrolytic dissociation of divalent symmetrical acids and bases, it is present, if the ratio  $\delta_1:\delta_2$  of the constants of the stagewise electrolytic dissociation is 4, which is approximately true with phenolphthalein and with crystal violet, since there is a connection between  $\delta_1:\delta_2$  and the ratios of the kinetic constants of the stagewise sequences of the electrolytic dissociation.

2. The reactivity of the group X is a dependent one in the manner that X reacts more slowly if the other X has already reacted--that is, is replaced by Z. Then,  $k_2 < u$ . This case appears to be the rule. It is, for example, realized in the alkaline esterification of the esters of the normal oxalic acid homologs and tartaric acid. It is also realized in the stagewise electrolytic dissociation of the symmetrical acids and bases, in that  $\delta_1:\delta_2$  is large as a rule and very frequently, very much larger than 4. (see E. Q. Adams, Journ. Am. Chem. Soc., 38(1915), 1503).

3. The reaction of the group X is an independent one in the manner that X reacts more rapidly if the other X has already reacted. Then,  $k_2 > u$ . This case is realized in the saponification of the carbonic acid ester. It appears to be realized, perhaps very generally, in the saponification of the ethers and esters of geminal glycols.]

Another question to be discussed on the basis of our reaction-kinetic finding is that of the characterization of the chemical nature of ethyl orthoformate. In this regard, in any case, one can say that the latter has to be eliminated from the class of esters and classified as an ether.

If R designates an alkyl and A, an acyl, then it is possible to establish three types of substances with an ethereal bonded oxygen atom with regard to the process of the hydrolysis and the all the rest of the chemical characteristics:

Type I (ethers):  $ROR'$

Type II (esters):  $AOR'$

Type III (anhydrides):  $AOA'$

This separation is not to be understood as a fundamental one but rather probably only as a gradual one, since, as P. E. Verkade [13] has shown, there is extensive agreement between the carbonic acid, on the one hand, and alcohol, on the other hand, and with regard to the chemical behavior of the two substance classes--if one disregards the specific reactions of carbonic acids caused by the carbonyl group--there is no basic difference.

If, on the one hand, an analogy exists between acyl and alkyl, then there is, on the other hand, such an analogy between alkyl and hydrogen. The view of the hydrogen atom as the simplest alkyl of saturated hydrocarbons goes back to J. H. van't Hoff [14] and was recently explained convincingly, namely, by K. Kubierschky [15]. Our overview therefore includes the free carboxylic acids and limiting cases of the esters and alcohols and water, as limiting cases of ethers. The important reaction of the saponification or hydrolysis proves to be then a case of "ester interchange," wherein one understands the phenomenon that the substances with an ether oxygen in reaction with other substances with ether oxygen are able to exchange their acyls and alkyls.

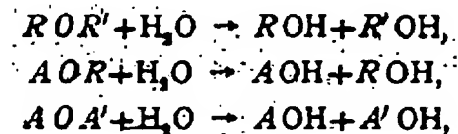
If one assumes multivalent alcohols and carboxylic acids as well as zwitter structures and the oxycarboxylic acids, then these substances are able to form internal ethers, esters, and anhydrides, in addition to the "external" ones. The carbonyl compounds, for example, are then to be understood as internal ethers of geminal glycols. Therefore, all organic compounds with an oxygen atom whose two valences are bonded to C or H fall into our overview.

Other organic compounds can be conceived, once again proceeding from our three types, derived in such a manner that R, A, RO, AO, or O are, stepwise, replaced by other analogous elements or element groups, wherein one arrives at compounds which, with regard to behavior and synthesis, exhibit a closer or more distant analogy with ethers, esters, and anhydrides. In this

way, one arrives at a nomenclature of the organic compounds whose original type is designated as the most general of our three types, the ester type.\*

Therefore, if clear transitions and continuities exist, then it is nevertheless recommendable, in the interest of the classification and the categorizing of individual substances into groups belonging together, to first stress what differentiates and separates. The showing of continuities and the search for laws for their gradation are tasks of later development.

The process of hydrolysis or saponification belongs among the reactions of our three substance types, which are also investigated quantitatively and therefore are known with the most accuracy:



the reactions, in a correspondingly strong dilution, take place more or less completely.

The principle of chemical kinetics regarding all possible reactions as also actually taking place, which comes from the general striving toward as uniform as possible an explanation of all natural events, leads us to assume the general time law of a secondary effect for the process of hydrolysis with unchangeable water concentration:

$$-\frac{dV}{dt} = k_a[OH']V + k_s[H']V + k_wV, \quad (11)$$

where V signifies the concentration of the hydrolyzing substance. The three rate constants  $k_a$ ,  $k_s$ ,  $k_w$  should be designated as the constants of the alkaline saponification, the acidic saponification, and the aqueous saponification.

The concentrations  $[OH']$  and  $[H']$  are not independent of one another, but rather linked by the following relationship:

$$[H'] [OH'] = w, \quad (12)$$

wherein it should be noted that the reaction leading to this equilibrium condition is established, according to experience, at an outstanding rate, so that the equation (12) is always fulfilled.

From (11) and (12), it can readily be seen that with a certain acidity, the rate of saponification  $-dV/dt$  must be a minimum. We experience the minimum condition if after inserting  $[OH']$  from (12) into (11), we differentiate the latter equation according to  $[H']$  and set the derivation equal to zero, wherein we receive the following:

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\* It would be very appealing to go into more detail regarding the "ester nomenclature" of the organic substances. I will postpone this until more experimental material, above all, rate measurements are available. The "reactivity" of the substances, the "mobility" of the atom and groups find their exact expression in the rate constants, wherein one has to consider that, as is known, the occurrence or nonoccurrence of a conceivable reaction in organic chemistry is far more frequently based on kinetics than energy, from which the importance of chemical kinetics for organic chemistry may be deduced. (A. S.)

$$[\text{H}^+] = \sqrt{\frac{k_a}{k_s}} \quad (13)$$

We can also write the condition (13) in the following form:

$$\frac{[\text{H}^+]}{[\text{OH}^-]} = \frac{k_a}{k_s} \quad (14)$$

which says that the rate of saponification is a minimum, if  $[\text{H}^+]$  behaves relative to  $[\text{OH}^-]$  like the constant of the alkaline saponification to the constant of the acidic saponification.

If we conceive of the saponification taking place with a constant acidity, perhaps regulated by a suitable buffer, then its minimum rate is given by the following equation:

$$\frac{-dV}{dt} = 2k_m V + k_w V_A \quad (15)$$

where  $k_m$  has the following meaning:

$$[\text{OH}^-]k_a = [\text{H}^+]k_s = k_m \quad (16)$$

On the other hand, there are two maximum values of rates of saponification, whose conditions can be approached by using solutions as alkaline as possible, or as acidic as possible; in this undertaking, however, one encounters limits, theoretically and practically.

The task of the kinetics is to determine all three saponification constants numerically, at least according to the order of magnitude. Relatively high values of one or the other of the constants can be easily measured, or if the pertinent reaction is immeasurably fast, can be easily determined. The case is different with relatively small values.

If a small constant of the water saponification is to be measured, then one will bring about the condition of the minimum rate. Then,  $k_w$  will still have to be measured, if it is of the same order of magnitude as  $2k_m$  [see equation (15)]. If  $k_w \ll 2k_m$ , then there is no prospect of being able to determine its value.

For the purpose of measuring a relatively small  $k_a$  or  $k_s$ , one will approximate the conditions of the maximum rates. The case that one cannot measure, for example,  $k_s$  in a strongly acidic solution, because even under this condition,  $k_s [\text{H}^+]$  is small, in comparison to  $k_a [\text{OH}^-]$ , is hardly expected according to previous experiences which have been gained with regard to the order of magnitude of the constants. According to these experiences, the range of the saponification constants, although large, is substantially smaller than that of the realizable acidities of around 14 powers of ten. In the most extreme case, therefore, one will be able to determine a halting of the saponification and thus the inability to measure  $k_s$  as a result of its smallness.

On the other hand, it may happen that one cannot get any idea regarding the order of magnitude of  $k_s$  because even in very acidic solution, is small in comparison to  $k_s [\text{H}^+]$ . Then,

occasionally, by adding an inert solvent, it is possible to shift the ratio  $k_s [H\bullet]:k_w$  enough, in favor of  $k_s [H\bullet]$ , so as to at least be able to establish the fact of the existence of an acidic saponification.

If we now survey the saponification of our three substance types with ether oxygen atoms, with regard to the absolute and relative values of  $k_a$ ,  $k_s$  and  $k_w$ , then one can state the following on the basis of previous observations and measurements.

Carboxylic acid esters. The constant of the alkaline saponification is very large and very different with the individual esters. For example, for the first methyl of the oxalic acid ester, it is of the order of magnitude [16]  $10^6$ ; for a large number of other methyl esters, the order of magnitude 1 and below.

The constant of the acidic saponification is small; with the various esters, not very different, of the approximate order of magnitude  $10^{[illegible]}$  and below.

The saponification rate minimum is, accordingly, in the vicinity of the neutral point, but always on the acidic side of the sample, for example, for ethyl acetate with  $[H'] = 3 \times 10^{-6}$ .

An aqueous saponification can generally not be determined--which says that a possible  $k_w$  is, under all conditions, small in comparison to  $k_a[OH']$  or  $k_s[H\bullet]$ . If measurements are present in the saponification minimum [17], they are an argument for a vanishingly small  $k_w$ , even in comparison to  $2 k_m$  [equation (15)]. It would be desirable to increase these measurements and in particular to extend them to esters with extreme saponification rates.

Alkaline, in addition to acidic saponification, with nondetectable aqueous saponification and  $k_a > k_s$  require, with the carboxylic acid esters, a sharply pronounced saponification minimum in the area of the weakly acidic reaction, as can be seen from curve II of the figure (abscissa acidity, ordinate reaction rate for  $V = 1$ , both in a logarithmic count) on the ethyl acetate as an example.

The relations between the three constants, explained here, are valid, as a rule, only for the carboxylic acid esters. With sulfonic acid esters and mineral acid esters, the conditions are substantially different [18].

However, with the carboxylic acid esters also, there are remarkable deviations from the rule. Thus, H. Johansson and H. Sebellus [19] have been able to detect a measurable aqueous saponification, in addition to an immeasurably rapid alkaline saponification\* and a measurable acidic saponification during the hydrolysis of the glycolide to glycolglycolic acid and the

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\* In the meantime, we were able to measure this rapid reaction so that now an ester is present in the lactide, of which all three constants  $k_a$ ,  $k_s$  and  $k_w$  are known according to the numerical value. We will soon report on our measurements.



lactide to lactolactic acid. The case of a carboxylic acid ester saponification, therefore, is present here, in which  $k_w$  can no longer be neglected, in comparison to  $[H^+] k_s$ .

As regards lactones,  $\gamma$ -lactones behave normally--that is, like the majority of the other carboxylic acid esters. As concerns  $\beta$ -lactones, on the other hand, the same researchers [20] were able to show particularly extreme deviations from normal behavior, if the hydrolysis of the  $\beta$ -lactones is not catalyzed by the hydrogen ion (or is catalyzed only a little).

With regard to the valid relation  $k_w \ll [H^+] k_s$ , the  $\beta$ -lactones already bring to mind the acid anhydrides.

Carboxylic acid anhydrides. The saponification or hydration of carboxylic acid anhydrides [21] is characterized by a high value of the constant of the water saponification. For example,  $k_w = 0.17$  for acetic anhydride at  $25^\circ$ , corresponding to a mid-point of around 4 min. In comparison to this amount,  $[H^+] k_s$  is difficult to validate, and the claim by A. C. D. Rivett and N. V. Sidgwick [22] that the hydrogen ion does not accelerate the hydration of acid anhydrides is easily understandable. On the other hand, K. J. P. Orton and M. Jones [23] are able to state that this hydrolysis is also accelerated by the hydrogen ion, although not as obviously as the ester saponification. The two researchers have also shown that the acids are, namely, very effective catalysts in water-poor media. In addition to the water saponification, therefore, the acidic saponification of the anhydrides is certain.

The acceleration of the hydration of anhydrides by acids (hydrochloric acid, sulfuric acid), moreover, is very clearly obvious also from older observations of a more qualitative nature [24].

The hydroxyl ion is an extraordinarily effective catalyst for the hydration reaction. The constant of the alkali saponification could not yet be determined up to now [25]. The difficulties lie less in the high value of  $k_a$  than in the magnitude of  $k_w$ , i.e., are of a similar type as those which oppose the determination of  $k_s$ . Since the saponification in a medium-strong acidic solution is a purely aqueous saponification,  $[OH^-] k_a$  must be small in comparison to  $k_w$  in these solutions. Therefore it would be easy to reduce  $[H^+]$  in such a way that  $[OH^-] k_a$  is large in comparison to  $k_w$ ; then  $[OH^-] k_a + k_w$  is all the larger, however, because  $k_w$  has, in fact, a high value and thus the reaction arrives at the limit of measurability. One has to reckon with these difficulties, therefore, in the measurement of  $k_a$ . In any case, it is already possible to say today that the  $k_a$  of slowly alkaline-saponifying anhydrides is approximately as large as the  $k_a$  of rapidly alkaline-saponifying esters.\* Therefore, the reactivity of an acyl A with regard to the

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\* I hope to be able to report soon on the alkaline saponification of anhydrides, at least as concerns the order of magnitude of  $k_a$ . (A. S.).

alkaline saponification in the anhydride AOA' is generally larger than in the ester AOR, so that anhydrides undergo alkaline saponification more rapidly, on average, than esters.

According to what has been said, the saponification curve of carboxylic acid anhydrides has approximately the course of curve III of our figure. Since the ratio  $k_a:k_s$  has a greater value than with the esters, the saponification minimum is shifted more toward the acidic side and as a result of the relation  $k_w \ll 2k_m$ , moreover, completely leveled.

Ethers. In comparison to esters and even more, in comparison to carboxylic acid anhydrides, ethers are very frequently, but not always, characterized by great reactivity. This low reaction capacity is manifested also in their behavior in the hydration or saponification process. Many ethers react with water, only very slowly, to form alcohol and this slow reaction is very probably an acidic saponification.

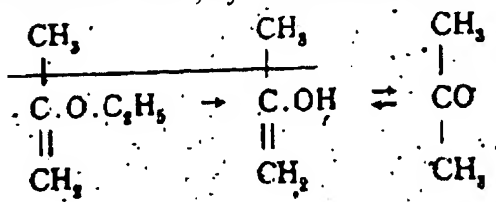
The oldest pertinent observations on ethyl ether are owed to A. Lieben [26]. Pure ether exhibits an iodoform reaction as a result of alcohol formation, in the presence of water, after a few months, more rapidly at  $100^\circ$  in a sealing tube. The circumstance that basic bodies, such as lime and caustic potash, do not attack the ether according to Lieben, whereas acids and salts change it, is an argument, with some probability, that the reaction with water is not a purely aqueous saponification either, but rather an acidic saponification, caused by the hydrogen ions of the water. It is therefore always  $[H^+]k_s > k_w$ .

That the hydrolysis of ethers is an acidic saponification follows from numerous observations of rapidly hydrolyzing ethers and from some measurements. The value of the constant  $k_s$  is very dependent on the nature of the alkyl. According to Eitekkoff [27], the ethers of tertiary alcohols are saponified more rapidly than the ethers of secondary alcohols; the latter again more rapidly than the ethers of primary alcohols; the ethers of unsaturated alcohols saponify more rapidly than the ethers of saturated alcohols.

Enol ethers [28] hydrolyze particularly rapidly under the influence of acids, or the hydrogen ion. Thus, vinyl ethyl ether is smoothly split into alcohol and aldehyde, according to Wislicenus [29], by allowing it to drip into dilute sulfuric acid:



According to A. Faworsky [30], isopropenyl ethyl ether is completely broken down into alcohol and acetone, rapidly and when cold, by 1% sulfuric acid:



Just as the ethers of tertiary alcohols hydrolyze more rapidly than the ethers of secondary alcohols, the ethers of tertiary enols also appear to react more rapidly than the ethers of enols whose hydroxyl is secondarily bonded.

The greater hydrolysis rate of enol ethers, in comparison to the lower rate of ethers of unsaturated alcohols, corresponds to the much greater influence of the  $\alpha$ -substitution, in comparison to the  $\beta$ -substitution.

In contrast to the rapidly hydrolyzing ethers of tertiary enols, phenol ethers are characterized by a great stability, a sign that not only the type of bonding of the alcohol group, but rather the entire core structure of the alkyl is decisive for the reaction rate.

Furthermore, aldehyde and ketone acetals have an ether nature.\* They are rapidly hydrolyzed in the presence of acids to alcohol and aldehyde, or ketone [31]. Here too, acetals of ketones appear to react more easily than those of aldehydes [32].

Following acetals, polysaccharides and glycosides should be noted. Their hydrolysis, like the much investigated cane sugar inversion, or the splitting of salicin into dextrose and saligenin [33], are acidic saponifications, in that the hydrolysis rate is proportional to the hydrogen ion concentration.

The ether character in carboxylic acid ethers, which have three alkoxy groups bonded to the same carbon atom, appears potentiated to a certain extent. Acidic saponification takes place here, as we were able to show for one case, at a great rate in a neutral solution also; indeed, this was even possible in a weakly alkaline solution, at a noticeable rate.

The designation of alkylated orthocarboxylic acids as esters is thus not justified. The hypothetical parent substances also bear their name incorrectly; they should be properly designated as geminal glycerols; the first member  $\text{HC}(\text{OH})_3$  should therefore be called a methenyl glycerol [34].

If one places the value 70,000 for methenyl glycerol ethyl ether, 0.01 for the sugar cane inversion [35], and the surely very small value of the acidic ethyl ether hydrolysis, which has not yet been quantitatively measured, in parallel, the one obtains an idea of the range within which the  $k_s$  of the ether saponification can fluctuate.

This range surely does not stand, to an extent, according to the range of  $k_a$  in the ester saponification and is supposedly just as comprehensive as the range of  $k_a$  of the anhydride saponification.

Reactive ethers are also characterized by a large  $k_s$ , like the most reactive anhydrides are by a large  $k_a$ . Esters hold the middle; their reactive representatives have high values of  $k_s$  and  $k_a$ ,

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\* At present, we are busy with the measurement of the hydrolysis of acetals and acyl derivatives of geminal glycols, the latter having a natural ester nature. (A. S.)

which, however, supposedly remain behind, measured on the values of  $k_s$ , or  $k_a$  of reactive ethers, or anhydrides.

The general reactivity of ethers, esters, and anhydrides runs symbatic to the saponification rate. The rapidly saponifying representatives of these substance classes are therefore also the most effective alkylation or acylation agents. They are used in the synthesis. The slowly saponifying agents are, on the other hand, of practical importance as inert solvents.

According to the numerical values of the saponifying constants, the ethers of saturated, primary alcohols, above all, are taken into consideration for this purpose.

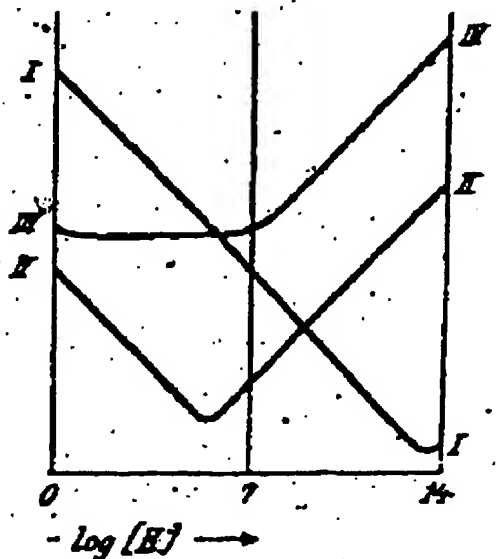
As concerns  $k_a$  and  $k_w$  of the ether saponification, there are no signs for a noticeable water saponification, to the extent that measurements are available. Similarly as with the esters, therefore,  $k_w$  should probably be small also, in comparison to  $[H^+]k_s$ .

On the other hand, signs of an alkaline saponification are present at times, even though the areas where ethers predominantly undergo an alkaline saponification hardly fall any longer into the range of aqueous solutions.

Thus, the phenol ethers are split with a longer heating with alcoholic alkali or by the alkali melt [36]. Ethers of multivalent phenols are partially or stagewise saponified, just like the esters of multivalent carboxylic acids [37].

In any case, the  $k_a$  is very small in comparison to the  $k_s$  with the typical ethers, so that the saponification minimum should lie in strongly alkaline areas and, from time to time, should not even be realizable. From constancy reasons, however, one should be able to infer a saponification minimum.

Curve I of the figure shows the course of the saponification curve of the ethers, as we, to some extent, are justified in assuming it, on the basis of our previous experience, as typical for this substance class.



If we consequently arrange the three substance types with the ether oxygen atom into the following series:

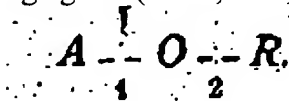
ethers, esters, anhydrides,

then the numerical values of  $k_w$  and the ratio  $k_a:k_s$  increase in the same sequence, whereas the saponification minimum is shifted from the area of the strongly alkaline reaction into the area of the acidic reaction and at the same time, flattens out more and more.

It was already stressed that all gradations are able to appear here. Thus, the phenol ethers impart the transition from ether to the slowly saponifying esters; the lactides and  $\beta$ -lactones, the transition from esters to carboxylic acid anhydrides. It will be possible to frequently find such transitions with a further study of the saponification phenomenon.

Of the three substance types, esters have been investigated the best and accordingly the theory of ester saponification\* has flourished the most. Every new standpoint will be able to cast new light also on this much discussed problem. The question is whether this does not apply also to the standpoint of the analogy of the three substance types with the ether oxygen atom, assumed by Verkade and, in the present case, also by us.

As van't Hoff has already explained [38], the ester AOR has two places in the molecule on which the attack of the saponifying agents (water, acid, base) can take place:



He suspects that during the saponification by alkali, the attack takes place at site 2 and during the saponification by acids, at site 1, and supports his suspicion on the status of investigations at the time, wherein the rate during the alkaline saponification was to be determined primarily from the nature of the alkyl and, during the acidic saponification, on the nature of the acyl.

The material available to van't Hoff is quite insufficient. One needs only to look at the values of  $k_a$  for the methyl ester of formic acid, acetic acid, benzoic acid, oxaminic acid\*\*, oxalic acid, malonic acid, sebacic acid, etc., in order to immediately see how enormously great is the influence of the acyl during the saponification with bases. Thus, van't Hoff's suspicion collapses.

From the fact wherein  $k_a$  is very large, in comparison to  $k_s$  with acid anhydrides, which have only site 1, and very small at that, in comparison to the ethers which have only site 2, one

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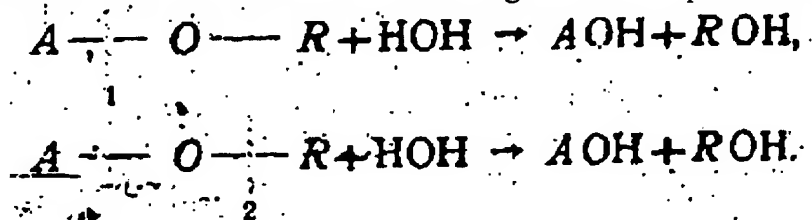
\* References to comprehensive explanation of these theories may be found in H. Johansson and H. Sebelius, Ber. Chem. Ges., 52 (1919), 747, Footnote 3.

\*\* The publication of an investigation on the oxaminic acid ester saponification is taking place approximately simultaneously. (A. S.)

would rather conclude that during the ester saponification by alkali, the attack takes place at site 1 and, by acids, at site 2. Therefore, exactly the opposite of the van't Hoff hypothesis.

One would proceed more correctly, however, if the view is again adopted, wherein every possible reaction actually takes place. Then it must be assumed that with all three types of ester saponification (alkaline, acidic, and aqueous saponification), the attack takes place at both sites 1 and 2, since anhydrides that have only site 1 de facto follow all three saponification routes, and ethers that have only site 2 follow at least basically all three saponification routes.

For the esters--and analogous for the "mixed ethers" and "mixed anhydrides"\*, reflections which one can generally make and, in a similar manner, has also repeatedly made for substances with two reactive groups are then valid. The saponification of the ester AOR takes place according to the two secondary reactions or--because the latter are identical and different only with respect to their "reaction mechanism"--according to the two "quasisecondary reactions":\*\*



If  $x_1$  signifies the conversion and  $k_a'$ ,  $k_s'$ ,  $k_w'$ , the three constants of the first reaction;  $x_2$ ,  $k_a''$ ,  $k_s''$ ,  $k_w''$ , the corresponding variables of the second reaction, then the following is valid for the only measurable summation rate:

$$\begin{aligned} \frac{dx}{dt} &= \frac{d(x_1 + x_2)}{dt} = \\ &= (k_a' + k_a'')[\text{OH}'](a - x) + (k_s' + k_s'')[\text{H}'](a - x) + (k_w' + k_w'')(a - x), \quad (17) \end{aligned}$$

if  $a$  is the starting concentration of the ester.

A comparison with equation (11) gives the following relations for the constants  $k_a$ ,  $k_s$ ,  $k_w$  of the saponification of the ester AOR:

$$\left. \begin{array}{l} k_a = k_a' + k_a'' \\ k_s = k_s' + k_s'' \\ k_w = k_w' + k_w'' \end{array} \right\} \quad (18)$$

\* This mode of designation appears to us not only shorter, but rather also more correct than the usual one: "mixed ethers" and "mixed anhydrides."

\*\* If the inequality of the two halves of the molecule is not attributable, like here, to the two ligands, but rather to the nonsymmetry of the nucleus, that is, if the substance with the unequal halves is of the formula X-AB-X, then actual secondary reactions take place with secondary effects.

If the two reactive groups bonded to the ether oxygen atom are identical, then a "pure ether" ROR or a "pure anhydride" AOA is present, and  $k_a' = k_a'$ , etc., is necessary and accordingly:

$$\begin{aligned} k_a &= 2k_a' = 2k_a'', \\ k_s &= 2k_s' = 2k_s'', \\ k_w &= 2k_w' = 2k_w''. \end{aligned}$$

Then  $0.5 k_a$ ,  $0.5 k_s$ ,  $0.5 k_w$  signify the rates at which a certain group from the pure ether or the pure anhydride saponifies, or the "group rate." They are, of course, half as great as the rates  $k_a$ ,  $k_s$ ,  $k_w$ , at which one or the other of the identical groups react.

With pure ethers and pure anhydrides, the group constants  $k_a$ ,  $k_s$ ,  $k_w$ , etc., are given, therefore, with the experimentally determinable constants  $k_a' = k_a'' = 0.5 k_a$ ; with mixed oxides, they remain unknown.

The question is now whether from the constants of the two pure oxides  $XOX$  and  $X'OX'$ , one may infer the constants of the mixed oxides  $XOX'$ .

This is readily possible in the limiting case that the reactive groups react uninfluenced and independent of one another. If, therefore, the  $X$  is saponified out, at the same group rate, from the  $XOX$ , as from the  $XOX'$ , and the  $X'$ , at the same group rate, from the  $X'OX'$ , as from the  $XOX'$ , then:

$$\left. \begin{aligned} k_a &= 0.5(p_a + q_a), \\ k_s &= 0.5(p_s + q_s), \\ k_w &= 0.5(p_w + q_w), \end{aligned} \right\} \quad (19)$$

where the indexed  $k$  designates the constants and mixed oxide, and  $p$  and  $q$ , the constants of the two pure oxides.

Equations (19) state that the rate is equal to the sum of the group rates or that the rate of the mixed oxide is equal to the arithmetic mean from the rates of the two pure oxides.

If one tests the equations (19) with the aid of the measurements, then it is evident that they are not fulfilled in reality. If we take ethyl acetate as an example, then  $k$  would signify the saponification constant of this ester;  $p$ , the constants of acetic acid anhydride;  $q$ , the constants of ethyl ether. It is true that only the water constant of the anhydride is not known from the constants of the two pure oxides, according to the value, but one knows, with certainty, that  $q_a$  is very small, in comparison to  $p_a$ , and  $q_w$ , in comparison to  $p_w$ , and very probably, also  $q_s$ , in comparison to  $p_s$ . From this and from (19), it would follow that ethyl acetate should react half as

rapidly as the acetic anhydride on all three saponification paths. Not just that this is, by far, not true, but that the reciprocal ratios of the three saponification constants are quite different with the ester from the anhydride was further shown above.

Now, acetyl and ethyl are two groups lying far from one another, and it is perhaps to be expected from the very beginning that the condition which is the basis of the equations (19) is fulfilled all the better, the more similar, in a chemical sense, the two groups bonded on the bridging oxygen behave. We can cite as such a case the mixed anhydride of acetic acid and propionic acid measured by P. E. Verkade [39]. For 25°, the constants of the water saponification of the three substances are the following:

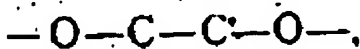
Acetyl oxide	Propionyl oxide	Mixed anhydride
0.1641	0.0857	0.1206

In this conceivably most favorable case, equation (19) is also fulfilled only in a very approximate manner:

$$0.5(0.1641 + 0.0857) = 0.1249 \sim 0.1206.$$

The two groups bound on the bridging oxygen -O- thus do not react independently of one another; they influence each other.

That was rather predictable according to the experience gained up to now with the esters of dibasic acids and diacidic alcohols. According to this experience, the condition of the uninfluenced reaction of two groups is all the better fulfilled, the longer the atom chain which links the two reactive groups with one another. The shortest chain which revealed a still uninfluenced reaction of the ligands in three cases (acidic saponification of oxalic acid ester, acidic and alkaline saponification of ethylene glycol ester) was the following chain:



whereas already the following chain (case of carbonic acid ester and orthoformic acid ether):



produced an extraordinarily strong reciprocal influencing of the ligands. Thus, one should expect, all the more, the latter for the chain -O-.

Instead of the equations (19), therefore, equations of the following form:

$$k = 0.5(pf + qg) \quad (20)$$

have to appear, where f and g are factors which manifest numerically the reciprocal influence of the groups X and X' in XOX'. The factors must be created in such a way that they approximate the value one to the extent that X and X' approximate identity, so that for X' = X, f = g = 1, in which limiting case (20) goes over into (19).



One will be able to progress in the search for corresponding functions for  $f$  and  $g$  when the three constants of a larger number of pure ethers and pure anhydrides and the corresponding mixed oxides become known some day. For the time being, there is only one single case where testing is possible: the already mentioned water saponification of acetic acid-propionic acid anhydride. Here it is possible to bring (20) in the following form:

$$k_w = 0.5 \left( p_w \sqrt{\frac{\delta_2}{\delta_1}} + q_w \sqrt{\frac{\delta_1}{\delta_2}} \right),$$

where  $\delta_1$  is the dissociation constant of the acid of the pure anhydride with the saponification constant  $p_w$  and  $\delta_2$  has the analogous meaning.

If one sets  $\delta_1 = 1.82 \times 10^{-5}$  and  $\delta_2 = 1.31 \times 10^{-3}$ , then:

$$k_w = 0.5 (0.1841 \times 0.8484 + 0.0857 \times 1.1787) = 0.1201,$$

that is, within the errors, identical with the experimentally found value  $k_w = 0.1206$ .

Since acetic acid and propionic acid are chemically very close, this agreement is temporarily not yet able to say very much.

The task of chemical kinetics must be to calculate in advance the rate of the saponification of all esters from as few natural constants as possible. If one considers that, as it was possible to show recently [40], in addition to the chemical nature of the reacting substances, their concentration is also decisive for the degree of the independence of the reacting groups and that the "constants" of the reaction rate are approximately constant only over small ranges, one will not be able to avoid agreeing with E. Faerber [41], who stated: "Every explanation, even that of a chemical reaction, is a never-ending task."

The saponification of the formic acid ethyl ester

The hydrolysis of methenyl glycerol ethyl ether to formic acid ester:



is followed by the saponification of the latter to formic acid:



Whereas the first reaction takes place at a noticeable rate only under the catalytic influence of the hydrogen ion and therefore is a typical ether saponification, the second reaction is catalyzed just as well by hydrogen ions, such as the hydroxy ion--that is, belongs to the class of ester saponifications.

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\* This form is closely related to Verdade's "reduced hydration constants."

Accordingly, there is an acidic and an alkaline saponification constant of reaction (2). The former was determined in the preceding as:

$$k_s = 0.192$$

The constant of the alkaline saponification was measured up to now according to two electrochemical methods and purely chemically, with the aid of an iodide-iodate solution as a hydrogen ion buffer.

In the latter solution, the reaction proceeds more slowly than desired. In an ammonia-ammonium salt solution, the rate can be measured at leisure, but there are concerns regarding this method, since secondary reactions with the formation of amide are not improbable. The even stronger alkaline reaction of the carbonate-bicarbonate buffer makes possible the measurability only with a large addition of bicarbonate. Under these conditions, those evils to which reference was already made in great detail have to be accepted. Nevertheless, taking into consideration that better methods are not known at the time, it appeared recommendable to measure the reaction in this way also.

The execution and calculation of the experiment was done in the same way as in the past [42].

#### Experiment 12

$t$	$a-x$	$k$
0	0.0592	—
8	0.0506	0.17
21	0.0362	0.18
46	0.0283	0.18
215	0.0080	0.19
		<hr/>
		(1) Mittel... 0.18

Key: 1      Average

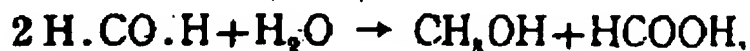
Using  $6 \times 10^{-11}$  for the second dissociation constant of the carbonic acid,  $[\text{OH}^-] = 1$ :

$$k_a = 1080,$$

a value is calculated which agrees sufficiently with the one found in the iodide-iodate solution, when one considers that the acidities in which the work was carried out here and there differ by three powers of ten.

The high value of  $k_a$  corresponds to the strength of the formic acid. The view that an ester saponifies, as a rule, all the more rapidly, the stronger its carboxylic acid, has been repeatedly expressed and as a whole, more or less confirmed by experience. On the other hand, the high value  $k_s$  of the acidic saponification is striking. The formic acid esters saponify acidically 20 to 30 times more rapidly than the acetic acid esters and homologs. The large  $k_s$  can be related with the acid strength, since the esters of much stronger acids than formic acid saponify acidically more slowly than the formic acid ester. The high value of  $k_s$  appears rather to be based in the chemical nature of the formic acid.

In fact, the formic acid is, both according to its behavior and its formula, just as much carboxylic acid (hydrogen carboxylic acid) as aldehyde (oxyformaldehyde). For the aldehyde nature of the formic acid, there is its easy oxidizability, which is completely in contrast to the difficulty with which acetic acid oxidizes; also the circumstance that, similar to the formaldehyde and certain aldehydes:



it is able to give the Cannizzaro reaction:



Formic acid

Formaldehyde

Carbonic acid

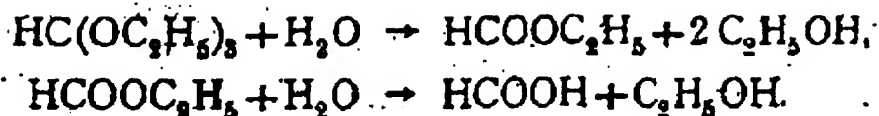
namely, if some of their salts are rapidly heated, and finally, the additional circumstance that according to M. Prud'homme [43] and its thermochemical data, it behaves like a mixture of carboxylic acid and aldehyde alcohol.

One will therefore hardly be mistaken if the rapid alkaline saponification of ethyl formate is attributed to its ester nature (formic acid ester), and the rapid acidic saponification, to its ether nature (ethoxy formaldehyde). As was shown in the preceding, the rapid acidic saponification is characteristic for the reactive ether. As an ether of a secondary alcohol and in view of the similar atom group as in methenyl glycerol ether, with which it is genetically related, the rapid acidic saponification of the ethoxy formaldehyde is not surprising.

Consequently, we have a substance present in ethyl formate which mediates the transition from esters to reactive ethers in a manner similar to the way phenol ethers form the transition from ethers to reactive esters.

## Summary

The hydrolysis rate of orthoformic acid ethyl ether was measured. It takes place via formic acid ester as a comprehensible intermediate stage:



The second reaction is a common ester saponification. Its already known constants of the acidic and alkaline saponification were recently measured.  $k_s = 0.192$  and  $k_a = 1080$  were found for  $25^\circ$ .

As concerns the first reaction, it was determined that it takes place immeasurably slowly in an alkaline solution. From this it follows that the ethyl orthoformate noticeably hydrolyzes neither by water alone nor under the influence of hydroxy ions.

On the other hand, the reaction takes place immeasurably rapidly in a strongly acidic solution. The production of formic acid from the ortho ether in mineral acid solution must therefore take place at a rate which is equivalent to the rate of the acidic saponification of ethyl formate  $k_s = 0.192$ . The measurements have confirmed this.

For the measurement of the rapid reaction, a hydrogen ion buffer from primary and secondary phosphate proved to be suitable. For the determination of the reaction progress, the produced formic acid ester was determined by analysis. The latter reacts with the acidity of the phosphate buffer and during the time of the experiments to an only very slight extent. Thus, the process of the hydrolysis of the ortho ether to formic ester was isolated, and at the same time, its course attained in a medium of constant acidity. The measurements produced a first-order reaction and the proportionality between rate and hydrogen ion concentration. The rate constant, relative to  $[\text{H}^+] = 1$ , has the value  $k = 70,000$ , which is unusually high in comparison with other acidic saponifications.

Following these experiment results and in connection with pertinent explanations by P. E. Verkade, the saponification of the three substance types, ROR', AOR, AOA' where R signifies alkyls and A acyls, was theoretically discussed and the proper classifications of ethyl orthoformate as ether type was indicated.

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